DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6010

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

FILE # 99-NWJ-20

April 27, 1999

Mr. Robert Occhifinto
President and Owner
NVE, Inc.
33-08 Newton Sparta Road
Newton, NJ 07860

Dear Mr. Occhifinto:

During an inspection of your firm located at 33-08 Newton Sparta Road, Newton, NJ from March 3 through March 12, 1999, our investigator documented deviations from current Good Manufacturing Practices (cGMP) for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, Part 211). These deviations were noted on the Form FDA-483, List of Inspectional Observations, issued to you at the close of the inspection.

The above stated inspection revealed that drug products manufactured at your facility are considered to be adulterated within the meaning of Section 501 (a) (2) (B) of the Federal Food, Drug and Cosmetic Act, in that the facilities and/or controls used in manufacturing are not in conformance with cGMP's as follows:

1) Your firm reprocessed Guaifenesin 200mg/Ephedrine HCl 25mg Tablets, Lot 9611213 and Pseudoephedrine HCl 60mg Tablets, Lot 9864165 and Lot 9864177 due to failing finished product content uniformity testing. Two additional lots Guaifenesin 200mg/Ephedrine HCl 25mg Tablets, Lot 9611211 and 9611220 were reprocessed without any documented reason in the batch record for the reprocessing. The reprocessing process, which includes milling whole tablets and additional blending, has not been validated to insure that batches will conform to established specifications. There was no data to demonstrate that the pharmaceutical products

would consistently meet quality attributes according to pre-determined criteria and specifications.

a. Reprocessing procedures were not reviewed by your quality control unit prior to initiation. These procedures should define the acceptance criteria for reprocessing and be approved by the quality control unit. Further, the reprocessed batches were not placed on stability to demonstrate that the reprocessed product will meet its established specifications throughout the product's shelf life. For example, Guaifenesin 200mg/Ephedrine HCl 25 mg Tablets, Lot 9611213 was compressed, on 12/7/98, after milling tablets that were originally compressed in 11/12/96.

b. Your firm did not document an investigation for Guaifenesin 200 mg/Ephedrine HCl 25mg Tablets, Lot 9611213, which was reprocessed due to failing content uniformity. Further, Lots 9611220 and 9611211 were also reprocessed but the reason was not documented. The investigation should determine if the failure is attributable to a production error and if other batches are associated with the failure.

c. Reprocessing was not performed according to an approved master record. Instructions were hand written directly on the batch record without approval from the quality control unit.

2) Your firm released Guaifenesin 200mg/Ephedrine HCl 25mg Tablets, Lot 9711119, which failed stage II Content Uniformity testing. The lot was released based on retest data without any justification for ignoring the original test results. An investigation at your contract laboratory did not reveal any cause for failure. Your firm did not conduct an investigation of production practices as required by your procedures in order to determine if the failure was attributable to a production error. It was also noted that your quality unit, who is responsible for releasing batches, was unaware of the failing results. The quality control unit did not note the failure during their review prior to releasing the batch.

3) Your investigation for Pseudoephedrine HCl 60mg, Lots 9864177 and 9864165 attributed the content uniformity failures to high humidity levels in the production area. However, there is no supporting data since the production room is not monitored for temperature and relative humidity.

4) The process validation for Guaifenesin 200mg/Ephedrine 25mg Tablets is inadequate in that two different blending instructions were found in the batch record for validation Lot 971112. Your firm was unable to determine which process was used during validation. Further, your quality control unit did not review or approve the completed process validation report.

5) Your firm failed to conduct an audit of your contract testing laboratory, [redacted], as required by your procedures.

The last audit was conducted in 1994. It is the responsibility of your quality control unit to insure that adequate laboratory facilities are used for release testing.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practices Regulations. You should take prompt action to correct the above violations and to establish procedures wherby such violations do not recur. Failure to do so may result in regulatory action without further notice such as seizure and/or injunction.

To date, we have not received a written response regarding observations listed on Form FDA-483 issued to your firm on March 12, 1999. You should notify this office in writing, within 15 working days upon receipt of this letter, of the steps you have taken to bring your firm into compliance with the law. Your response should include each step being taken that has been taken or will be taken to correct the violations and prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within the corrections will be completed. Please include copies of any available documentation demonstrating that corrections have been made.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts. In addition, pending new drug applications (NDA's), abbreviated new drug applications (ANDA's) or export approval requests may not be approved until the aforementioned violations are corrected.

Your reply should be directed to the Food and Drug Administration, Attention: Abita Nanda, Acting Compliance Officer, at the address and telephone number above.

Sincerely,

Edward H Woodruff for
Douglas I. Ellsworth
District Director